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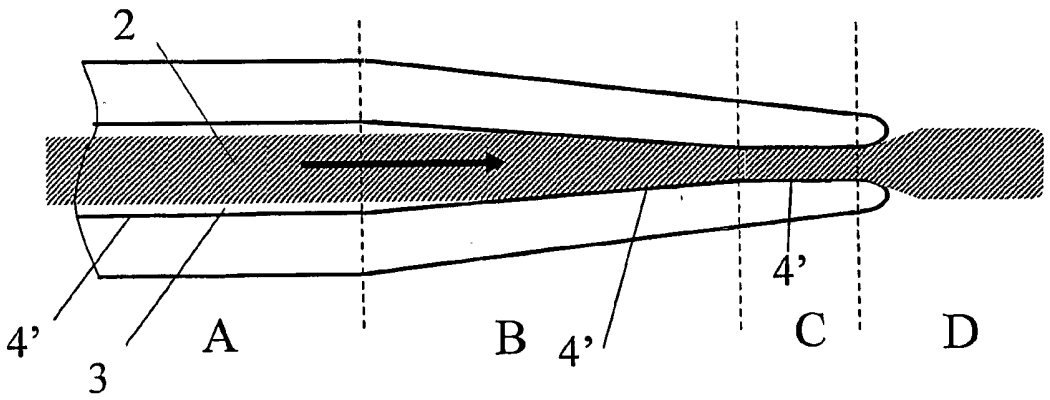

(57) Abstract: An implant and a system for implanting the implant are provided. The implant is formed from a fiber having swelling characteristics which assist in formation of a kinked, coiled and/or entangled bundle. The fiber is advantageously a hydrogel which undergoes radial compression prior to delivery into a target site in tissue. The system includes an introducer having an internal lumen and a constricted discharge orifice. A deformable fiber is slidably contained within the lumen in substantially fluid tight relationship with the discharge orifice. The lumen also contains a fluid which can be gas or liquid. In one embodiment, when pressure is applied to the fluid, the fiber is pushed through the discharge orifice, compressing he fiber in the constricted area. When the fiber passes out of the orifice, it expands radially, thus increasing its diameter. In a preferred embodiment, as the fiber expands, it does so anisotropically, thus causing the fiber to kink and/or coil. Hydraulic or pneumatic pressure generated by the introducer propels the fiber into a target site in tissue.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

FIBER IMPLANT SYSTEM FOR SOFT TISSUE AUGMENTATION

Background

Cross Reference To Related Applications

The present disclosure claims priority to U.S. Provisional Application Serial No. 60/468,202, filed May 6, 2003, entitled Fiber Implant System for Soft Tissue Augumentation, the entire disclosure of which is incorporated by reference herein.

1. Field of the Invention

The invention relates to surgical implants, and more particularly, to fibrous implants and systems for inserting them.

2. Description of Related Art

Implants of various types into soft tissues are used for many medical indications, such as tissue augmentation and/or reconstruction. For example, silicone implants for mammary augmentation or facial reconstruction are well-known. One problem of such implants is the need to form relatively large incisions to insert them. Such surgery can be traumatic and potentially lead to excessive scarring and other problems. The problem of large incisions may be solved by implanting dispersions of particles by injection through a needle to form bulking deposits in the target tissues. One example is augmentation of a urinary sphincter by injection of PTFE particles. Another example is intradermal injection of cross-linked collagen particles to smooth-out wrinkles. A problem with these types of "implants" is migration of particles out of the target tissues, particularly if the particle size is below a certain thresh-hold.

Attempts are being made to improve the state of the art relating to tissue implants. For example, a generally ball-shaped implant formed by insertion of a pliable fiber into tissue is described in U.S. Patent Nos. 6,296,632 and 6,299,590. These patents describe a device for application of the implant characterized by a tube and instruments which deliver the implant in fiber-shaped form through a distal opening in the tube. A fluid stream is generated by the instrument which may transport the fiber through the tube. The fiber may be wound around a bobbin and held in the device. Alternatively, a fiber that is not longer than the tube may be placed in the device so that a bobbin is not required. Fluid flows through the tube thereby transporting the fiber. Preferably, the fiber together with the fluid is discharged at the distal opening. The fluid can be a liquid or a gas. Alternatively, the fiber may be transported without the fluid using a propelled bobbin. The fiber is introduced into the body and when it encounters body tissue it folds upon itself to form a ball-shaped implant.

The implantation system described in the '632 and '590 patents may have several shortcomings. First, the random fiber bending into a generally ball-shape as described

therein may form a potentially unstable structure that can be disassembled, for instance, by pulling one of the free ends. A second disadvantage is that the random bending leads to a generally ball shaped implant which is suitable only for situations when the implantation site is a generally ball-shaped cavity or when the implant does not need to fill the cavity and conform to its shape. A third disadvantage is the relative size of the tube and the implanted fiber – the fiber is described as having a smaller diameter than the implantation tool, thereby requiring a implantation incision to be relatively large to accommodate the "hollow member" instrument. Another disadvantage occurs when it is necessary to extrude some fluid liquid along with the fiber. Even if the liquid is non-toxic and biocompatible, excess liquid can cause swelling of the tissue or form a pocket with conditions favorable for an infection. And finally, the fiber must be implanted into a pre-existing cavity since any contact between a tissue and the fiber causes the fiber to bend implying that this system is unsuitable for forcing the implant into a tissue. US Pat. No. 6,440,098 is directed to a device for implanting filamentous materials. As described therein, a thread-like implant is applied with a pressure-generating, fluid-containing means that is connected with a casing accommodating the thread to be implanted, wherein the casing empties into a channel. The thread to be applied is introduced into the distal end of the channel. Pressure exerted on the fluid is said to enable transport of the thread through the distal opening in the channel, where the thread is discharged to the outside, or into a tissue or hollowed out body. The diameter of the opening is said to essentially correspond to the threadlike material. The threadlike material is shifted through the opening via a pressure difference, during which no fluid stream is moved. The fluid is only used to hydraulically convey the hydrostatic pressure built up by a pressure generating means to the thread, which gets pressed out of the distal opening. Fluid is not envisaged as exiting from the opening along with the thread.

Surgical implants are formed from various materials depending on the requirements of the situation. In certain situations, hydrogel implants may have advantages over implants made from other plastics. For example, suitable hydrogels are characterized by:

- capability of substantially complete purification from residual monomers, initiators and other extractables;
- high biocompatibility resulting in a fine and stable or even non-existent implant encapsulation;
- high surface lubricity and low wet friction against a surrounding tissue; and
- permeability for aqueous liquids, nutrients and metabolites

(for review see: Hydrogels, in Encyclopedia of Pharmaceutical Technology (J. Swarbrick and J.C. Boylan, Eds), pp. 91 -117, Volume 18, Supplement 1; Marcel Dekker Inc., New York, N.Y., 1999).

Another advantage of hydrogels is their capacity for storing deformation in a contracted, dehydrated (or xerogel) state; and then returning to an expanded size and shape upon rehydration. Accordingly, hydrogels may be implanted in a partially or fully dehydrated deformed state and allowed to expand *in situ* by absorption of body fluids (e.g., Siebser, U.S. Patent 4,556,998). This is sometimes utilized for implantation of a device through a small incision, such as in the case of intraocular lenses (Knoll et al, US

Patent 4,919,662). The controlled expansion due to hydration can be utilized to stretch a slack tissue, such as vocal chords (Z. Kresa, J. Rems and O. Wichterle, Otolaryngology – Head and Neck Surgery, pp. 242-246, Volume 98, Number 3, March 1988), or for expansion of a cervical channel. Swelling pressure generated by hydration can be used for functional replacement of Nucleus Pulposus. Such a hydrogel device is described, for instance, in Stoy, U.S. Patent No. 6,264,695. Hydrogels can also be used for tissue augmentation, e.g., in the form of mammary prostheses or urinary sphincters.

Hydrogels can also be used for filling undesirable body cavities, such as varices of esophagus, veins supplying a cancer, i.e., as an embolic agent or for filling aneurisms. This goal can be difficult to achieve with solid pre-formed hydrogel implants because the space to be filled is irregular and poorly defined both in volume and shape. In such cases hydrogel is sometimes applied in a form of multitude of particles such as beads or discs. See, e.g., Berg, US Patent No. 5,116,378. A problem with particle implantation is the ability to retain the particles in the implant location. Particles can migrate out of their designated site and through the tissues. Small particles can be also phagocytosed and transported through the body via lymphatic pathways.

Hydrogels can also be implanted in liquid form. A liquid precursor (such as a monomer mixture or a polymer solution) is injected and then solidifies *in situ* via various mechanisms (e.g., polymerization or crosslinking reaction in two-component systems; photo-crosslinking or photopolymerization; or coagulation of solution in water-miscible non-toxic solvents, see, e.g., Stoy and Chvapil, US Patent No. 5,116,378.). The main advantage of this system is the delivery of the liquid through a very small incision (such as a hypodermic needle puncture) and filling the available space regardless its shape and size. However, these methods may have their own risks and limitations. In many cases, they involve either reactive chemicals or solvents with their own respective toxicological and regulatory problems. US Pat. No. 5,443,454 is directed to a catheter for embolectomy in which a liquid substance is delivered to the end of the catheter which is equipped with a spinning means for extruding the liquid in the form of a filamentous embolic material. In one embodiment, the liquid may be a photoreaction type liquid substance. One disadvantage, however, is that it may be difficult to expose the liquid to a source of light to initiate the photoreaction. In addition, polymerization may be an exothermic reaction, which could damage surrounding tissue. Moreover, as described therein, the photoreactive liquid contains an organic solvent. Unfortunately, systemic administration of organic solvents may create toxic conditions in the body.

There is a continuing need to develop safe and effective surgical implants that can be delivered to target locations using minimally invasive techniques. The present invention is addressed to that need.

Summary

An implant and a system combining advantages of pre-formed solid implants which can be implanted through a small incision or a puncture via a hypodermic needle or a catheter is provided. An implant is formed by one or more fibers having a length

substantially larger than the diameter. The fiber is implanted by extrusion through an introducer (such as a syringe or a catheter) by pressure of a fluid medium. In one embodiment, the fiber has, in its fully swelled state, an outside diameter larger than the inner diameter of the needle or catheter used for delivery. In a preferred embodiment, the fiber undergoes radial compression during movement through the needle or catheter. In turn, radial compression can cause a temporary partial expulsion of fluid from the fiber. The excess fluid from the compressed part of the fiber can serve as a lubricant facilitation of the fiber extrusion. The liquid lost by the fiber due to compression may eventually be replaced by liquid contained at the implant site. This feature allows extrusion of the fiber without extruding any substantial amounts of the propellant fluid at the same time. In addition, the fiber may be extruded into a target tissue under relatively high pressure. In one embodiment, the fiber and propulsion fluid are sterile. The fiber can be implanted by deposition in a generally linear form following puncture of a target site with an implantation needle. The fiber can also form an entangled mass in the target tissue. Decompression and rehydration of the fiber upon exit from the introducer can cause local fiber deformation that can be characterized as coiling, braiding and/or kinking. The self-coiling and kinking tendency can be further supported by selecting a fiber with a specific bias toward coiling, braiding, twisting and/or kinking. In a preferred embodiment, the fiber is made of hydrogel. In a further preferred embodiment, the fiber is capable of anisotropic expansion.

Brief Description of the Drawings

FIG. 1A illustrates a syringe containing fluid and a fiber within a hypodermic needle.

FIG. 1B illustrates the syringe, fiber and hypodermic needle of FIG.1A after activation of the plunger of the syringe.

FIG. 2A illustrates a syringe containing fluid along with a hypodermic needle and a fiber which is packed in the barrel of the syringe, extending into the hypodermic needle.

FIG. 2B illustrates the syringe, fiber and hypodermic needle of FIG. 2A after activation of the plunger of the syringe.

FIG.3 illustrates the end of a tube for dispensing a fiber along with a portion of a hydrogel fiber protruding from the end of the tube.

FIGS. 4A, 4B, 4C, and 4D illustrate examples of different packing configurations of long fibers for containment in an introducer.

FIG. 5 illustrates a spinneret, extruded fiber and a coagulation tube.

FIG.6 illustrates an example of an introducer which includes a syringe for holding and dispensing fluid, a syringe for holding a fiber, receiving fluid and for dispensing the fiber and fluid, a catheter, and a hypodermic needle.

FIG. 7 illustrates a syringe, hypodermic needle and fiber, wherein a portion the fiber has been extruded from the needle and has coiled.

Description of Preferred Embodiments

In accordance with the present invention, a fibrous implant can be inserted into a tissue or cavity in tissue under high enough pressure such that an implant is formed therein. The fibrous implant delivery device and the fiber cooperate to pressurize the chamber in which the fiber is contained, thereby propelling the fiber to a desired locus whether or not a cavity was present prior to delivery. In addition, the fluid in the container that holds the fiber does not, to any appreciable extent, pass into the tissue along with the fiber. Relatively high implantation pressure allows implantation of fiber implants into tissues with no pre-existing cavities (either natural or surgically formed). Such "relatively high implantation pressure" (otherwise referred to, e.g., as "high implantation pressure" or simply "high pressure") is any increase in pressure caused hydraulically or pneumatically as more fully described below in accordance with the present invention.

The fiber can be implanted by a deposition in a generally linear form following entry of the implantation needle into a desired locus. In one embodiment, the fiber is extruded while the needle is being withdrawn from the tissue thus depositing the fiber into the needle puncture. If desired, any excess fiber can be snipped off while the needle exits the tissue to make sure that the fiber does not protrude from the wound and provide a pathway for an infection. This can be further achieved or supported by an axial contraction of the extruded fiber.

The fiber can also form an entangled mass in the target tissue. Decompression and rehydration of the fiber upon exiting the introducer (such as a hypodermic syringe) causes local fiber deformation that can be characterized as self coiling, braiding and/or kinking that leads to a three-dimensional structure more stable than a fibrous ball formed by a random (unbiased) bending of a fiber described above relative to the prior art. In addition, according to the present invention, an entangled structure can be formed even in a relatively free space where the fiber does not meet any appreciable resistance by contacting tissue or other body components, such a blood during an aunerysm filling or an embolization. The self-coiling and kinking tendency of the fiber can be further supported by selecting a fiber with a specific bias toward coiling, braiding, twisting or kinking. Such fibers are generally anisotropic and may have a generally asymmetric cross-section. One example is a bicomponent hydrogel fiber including two or more materials with different hydration capacity and/or different axial expansion upon hydration. Another example is a naturally coiled hydrogel fiber that is temporarily straightened during the extrusion through an introducer.

The fiber is made of any material which will deform and swell in accordance with the conditions described herein. Both bioabsorbable and non-bioabsorbable polymers can be utilized. Bioabsorbable polymers such as lactide, glycolide, caprolactone, dioxanone, trimethylene carbonate, collagen are well known in the art. Other well-known polymers include polytetrafluoroethylene, crosslinked polyalkylacrylates, elastomeric polyolefins, polysiloxanes and polyvinylpyrrolidones. Hydrogels, as described below are particularly preferred. It is also contemplated that coatings can be applied to fibers used herein to increase hydrophillicity and lubricity. Such coatings are well-known, e.g., in the suture art.

In one embodiment of the present invention, a fiber made, for example, of hydrogel, is inserted in a dehydrated state into a hypodermic needle syringe, a catheter or similar introducer, and then loaded by hydration or imbibing an oleaginous liquid until it completely fills at least the narrowest part of the inner lumen of the introducer. The fiber in the narrowest part is compressed by virtue of its own swelling pressure. The loaded fiber is then extruded from the introducer into the implantation site by pressure of a sterile fluid medium, such as sterile isotonic saline. An example is shown in FIGs. 1A and 1B. In FIG. 1A, syringe **1** with plunger **6** is equipped with a hypodermic needle **4** and filled with sterile fluid medium **3**. Fiber **2** is deposited in the needle **4** and completely fills the narrowed lumen **7**. In FIG. 1B, pressure on the plunger **6** extrudes the fiber **2** into the implant site **5**.

In the embodiment shown in FIGs. 1A and 1B, a limited length of the fiber is delivered. It is also contemplated that a longer fiber can be placed in the syringe **1.** The fiber **2** is then deposited into the implant site **5** by the pressure of the fluid medium **3**. As long as the fiber **2** fills the narrowest part **7** of an introducer such as the hypodermic needle **4** prior to and during injection and the fiber 2 in the medium **3** is deformable enough to be squeezed through the narrow lumen **7**, then all fiber can be extruded before medium **3** can escape from the container **1**.

Thus, in a preferred embodiment, a hydrogel fiber for implantation is stored in a sterile fluid-filled container of the introducer, such as the barrel of a syringe. The hydrogel fiber is then extruded by the pressure of the fluid through a channel or an orifice such as a hypodermic needle, canula, or a catheter. The extrusion (or "injection") of the fiber can be performed directly into a tissue or a body cavity where it coils, kinks and forms an entangled mass generally filling the available space. One specific advantage of the present invention is that the fiber can be compressed into a cavity of nearly any shape (not only a generally ball shape). It also is contemplated that a hydrogel implant according to the present invention can be implanted in a manner that expands the target tissue or the pre-existing cavity. This can be accomplished by inserting a sufficient amount of fiber to exert positive pressure against the bounds of the cavity where the fiber is inserted. In some instances, the dehydrated fiber absorbs bodily fluid and expands to exert positive pressure as well. Another advantage of the present invention stems from the relatively high degree of pressure that can be generated by cooperation of the fiber and the delivery device. The high extrusion pressure allows addition of greater and greater amounts of fiber to increase the outward pressure of the implant against the cavity

wall. Similarly, the ability to generate sufficient positive pressure provides an efficient mechanism to transport the fiber into tissues where there was no pre-existing cavity. Some further advantages of the present invention are fibrous implants which are resistant to migration, improved implant stability and implantation through a minimally invasive technique. A preferred indication is tissue augmentation.

Another example of an embodiment of the present invention is schematically depicted in FIGs. 2A and 2B. As shown in FIG. 2A, pre-formed fiber **2'** is stored in a container such as the barrel of a syringe **1** filled with a fluid medium **3** and the fiber **2'** protrudes through a channel such as a hypodermic needle **4.** The fiber **2'** is compressed and partly dehydrated to completely fill at least the narrowest part of the lumen **7.** As shown in FIG.2B, when pressure is applied to the fluid, the increased pressure of the fluid **3** extrudes fiber **2'** through the channel **4** through the lumen **7** into the tissue **5** or tissue cavity **8.** The fiber **2'** then hydrostatically equilibrates with the tissue. It is preferred that substantially only the fiber is extruded through the orifice while the fluid substantially remains in the container at least until all fiber is extruded. However, a small amount of the fluid can escape along with the fiber during the extrusion. It is important, therefore, that the fluid is relatively non-toxic and biocompatible, such as isotonic saline. In addition, both fiber and the fluid should be sterile. It is preferred that the fiber is in substantial thermodynamic equilibrium with a fluid. As used herein, the terms "substantially" and "substantial" are intended to mean approximately or exactly.

The channel may be a simple bore of a tubing with an inner diameter smaller than the outside diameter of the fiber. Such tubing can be rigid such as a hypodermic needle; or flexible, such as in a plastic catheter. In other cases, the channel can taper down in a conical fashion, such as indicated in FIG. 3. FIG. 3 shows a fiber **2** penetrating in the direction of the arrow through the tapering tip of an injection tube such as a catheter **9** consisting of three zones, A, B and C to an external expansion zone D:

A is a cylindrical zone where the channel **4'** diameter is larger than the undeformed diameter of the fiber **2.** The fiber freely proceeds through this zone and is surrounded by the fluid medium **3.** If the pressure of the fluid medium **3** is higher than the pressure in the expansion zone **D,** extrusion of the fiber occurs.

B is a conical compression zone where the diameter of the channel **4'** decreases. The fiber compresses gradually and accelerates its movement along its path.

C is a cylindrical zone where the diameter of the channel **4'** is smaller than the undeformed fiber diameter. Fiber typically proceeds through this zone with axial velocity greater than the velocity through the zone **A.** In such instances, the two velocities are approximately in proportion to the square of ratio of fiber diameters in the two zones. In a preferred embodiment, fiber in this zone is lubricated by a very thin aqueous film. In the case of a hydrogel fiber, the liquid in the film is partly the fluid medium **3** carried along the fiber due to high wetability of the hydrogel with the aqueous liquid and liquid adhesion to its surface. In addition, some liquid can be squeezed out from the hydrogel due to the hydrogel compression. This liquid can be replaced later by the fiber rehydration from bodily fluids in the implanted state. This type of liquid film lubrication is an advantage of hydrogel fibers over hydrophobic elastomeric fibers.

D is the area where the fiber expands into the free space beyond the catheter and is deposited into the target site with decreased axial velocity.

The channel typically has a substantially circular cross-section. However, it can also have a cross-section of different shape, such as substantially square, rectangular, oval or elliptical. Various sections of the channel may have different cross-sectional aspects. If the fiber has a cross-section of a different shape than the shape of the channel the fiber should be sufficiently deformable to comply with the channel geometry and to have at least the same, but advantageously larger cross-section than the cross-section of the channel or its narrowest zone (e.g., the zone C in FIG. 3) so as to form a snug, substantially fluid-tight fit. It should be understood that the narrowest zone may be characterized as a constricted discharge orifice. The orifice may be located at the end of the lumen or it may be placed in a position recessed from the end of the lumen, such as, e.g., an interiorly disposed ring or other area of decreased diameter. It should be understood that the constricted discharge orifice can be any area which forms a substantially fluid-tight arrangement with the fiber that also causes compression of the fiber. Thus, e.g., the entire length of a hypodermic needle may constitute a constricted discharge orifice if it has a diameter that cooperates with the fiber to form a substantially fluid-tight arrangement. In addition, a lumen, or portion of the lumen, may have the same internal cross-sectional dimension as the constricted discharge orifice to form a substantially fluid-tight seal with an internally disposed fiber.

The fiber is preferably lubricious enough to slide through the channel easily. This sliding can be further facilitated by lubricious non-toxic additives in the liquid medium, such as polyvinylpyrrolidone, hyaluronic acid, glycerin or a dextran. In a preferred embodiment, a hydrogel fiber has equilibrium liquid content in isotonic saline of at least about 30% by weight, preferably over about 50% by weight. The hydrogel fiber should have sufficient strength and deformability to withstand the injection safely, i.e., it should not be substantially degraded under the conditions of injection and implantation. Relative tensile deformation over about 75% is usually sufficient but relative deformations over about 150% are preferred. Particularly preferred are hydrogel fibers with equilibrium water content about 80% by weight and tensile relative deformation over about 200% at full equilibrium hydration.

Suitable hydrogel fibers for the implantation can be made from various hydrogels well known to those skilled in the art. Preferred implantable hydrogels are physically cross-linked hydrogels cabable of forming two-phase structures such as partially hydrolyzed or aminolyzed polyacrylonitriles, polyvinylalcohol, segmented polyurethanes, polyureas and polyesters. One main advantage of preferred hydrogels is the capability to achieve high hydration while maintaining good mechanical properties that are usually required for the implantation through a small incision. Particularly preferred are hydrogels based on partially hydrolyzed and/or aminolyzed polyacrylonitrile, including but not limited to hydrogels described in U.S. Patent Nos. 3,987,383; 3,926,930; 3,948,870; 4,420,598; 4,107,121; 4,366,206; 4,374,175; 4,379,874; 4,943,618; 5,252,692 and 6,232,406, each of which being incorporated herein by reference.

Examples of other suitable hydrogels are:

- Physically cross-linked polyvinylalcohol (PVA) hydrogels such as those described in U.S. Patent No. 4,663,358, incorporated herein by reference.
- Hydrophilic segmented polyurethanes and/or polyureas
- Hydrophilic segmented polyesters
- Polymers and copolymers of acrylic and methacrylic acid derivatives comprising esters of polyhydroxy compounds such as ethyleneglycol, diiethyleneglycol, triethyleneglycol or glycerol
- Hydrogels made from cross-linked natural polymers such as albumin, collagen, alginate or hyaluronic acid.

Those skilled in the art may utilize any known suitable hydrogels among these groups or other known hydrogels or hydrophilic polymers (such as gelatin, agarose, cellulose derivatives, collagen or composite fibers containing a hydrogel component).

Certain embodiments contemplate use of hydrogels that can exist in two forms, one with a lower equilibrium hydration for implantation and the other with a higher equilibrium hydration for indwelling after the implantation (hydrogels with 2-stage hydration). The low-hydration form is used for implantation and then converted into a more highly hydrated form by changes in its environment. For example, such conversion may be provided by an increase in temperature from ambient to the body temperature. There are numerous hydrogels with this property, including crosslinked block copolymers of polyethylene glycol with polypropylene glycol; polyvinylmethyl ether; poly(N-isopropyl acrylamide) and other compositions known to those skilled in the art. It is also contemplated that hydrogels with hydrolyzable pendant groups or cross-links or main chain sections in which interaction with hydrolytic conversions of certain groups into more hydrophilic groups increases polymer hydrophilicity or decreases crosslinking density may be utilized. There are numerous examples of such polymers with controlled biodegradability and bioerodibility that are well known to those skilled in art. Examples of such polymers are poly(acetyl-2-hydroxyethyl methacrylate); polyvinylalcohol grafted with polylactic acid, crosslinked proteins such as crosslinked gelatin, etc. Some of these hydrogels have low swelling due to ionic crosslinking by polyvalent counter-ions or inter- and intra-chain crosslinking of amphoteric hydrogels. Further examples are hydrogels with certain pendant groups including carboxyl, amide and amidine in mutual 1,3 positions. Such groups can undergo reversible intramolecular cyclizations to form groups like cyclic amidines, cyclic semiamidines, cyclic imides, cyclic imidines etc. Hydrogels with these cyclic structures have lower swelling. Once these cyclic structures are opened to create individual hydrophilic pendant groups, equilibrium swelling increases. Such structures are disclosed, for instance, in U.S. Patent Nos. 3,987,383; 3,926,930 and 3,948,870.

Preferably, the surface of the fiber is lubricious due to a high surface hydration. Particularly preferred are methods that can increase concentration of carboxylate groups on the hydrogel surface. Surface hydration of hydrogels can be improved by reacting

hydrogel articles with suitable reactants, such as hydroxides, as described, for instance, in U.S. Patent Nos. 4,366,206 or 5,939,208, each being incorporated herein by reference.

It is also known that hydrogels can be used as a carrier for local or sustained delivery of medicinal agents, such as growth factors, cytostatics, anti-inflammatories, antihistamines, antifungals, or antibiotics. Hydrogel implants in accordance with the present invention can by used for sustained and controlled drug delivery in the same fashion. In certain embodiments, a fluid medium contains dissolved medicinal agents such as antimicrobials, preservatives, antibiotics, steroids, growth factors, dyes and the like. The bioactive molecules may be incorporated into the hydrogel fiber by absorption and partition. It is also contemplated that implants according to the present invention can incorporate a radiopaque substance to allow the implant to be visible during and/or after implantation. Such radiopaque substances are well-known to those skilled in the art. For example, an implant can be made detectable by X-ray by using suitable X-ray markers. For example, gold flakes, gold powder, platinum whiskers or tantalum powder can be dispersed within the hydrogel prior to implantation.

Typically, one fiber is implanted at a time through one needle or catheter. However, more than one fiber can be injected to a single site to achieve a desirable effect.

During implantation, fiber **2** or **2'** is sometimes transformed from a relatively orderly arrangement in the container into a more random shape in the implant site. For instance, a straight fiber in the container can become a kinked, coiled and/or entangled fiber bundle in the implantation site. A relatively short fiber, such as the ones depicted in FIGs. 1A, 1B, 2A or 2B, can be extruded rather easily from a loose random loop without a great risk of premature kinking. Longer fibers, however, are advantageously properly and orderly arranged in the container to allow continuous extrusion. Typical orderly arrangements are, for example:

1. Zig-zag packing, parallel to the channel;
2. Zig-zag packing transverse to the channel;
3. Single- or multi-layered helix;
4. Spools or reels;

and other arrangements from which a continuous fiber can be unwound and deployed without any kinking prior to extrusion.

In a preferred embodiment, both fiber and the propulsion fluid are sterile. For some materials, sterilization of the fiber can be performed in dehydrated state by heat, steam, gamma irradiation, electron beam irradiation or by ethylene oxide. Sterilization of the dehydrated fiber and the propulsion liquid may be performed separately, and the sterile components are then combined during or prior to the implantation. In an alternative embodiment, sterilization of all components can be performed simultaneously by a suitable means, such as heat, chemical agents or irradiation.

Several exemplary arrangements are depicted in FIGS. 4A (zig-zag parallel to the channel), 4B (zig-zag transverse to the channel), 4C (coiled) and 4D (wound on a spool).

The fiber in the introducer is preferably sterile and ready for the delivery into tissue. The fiber in this "Delivery-ready state" has certain properties that are not necessarily the same as properties in the implanted state where the fiber is in equilibrium with body fluids. The fiber in equilibrium with the fluid medium has certain hydration, anisotropy index, diameter and length in this state hereinafter referred to as the "Delivery State". In the case of hydrogel fibers, "hydration" here shall mean the liquid content expressed as the volume fraction of liquid inside the gel. "Anisotropy index" means the ratio of relative expansion in diameter and length. Anisotropy index of isotropic fiber equals about 1. Anisotropic fibers can have anisotropy index higher that unity, sometimes equal to 5 or even higher. To maintain the anisotropy index different from unity, fiber can be prepared and stretched during the dehydration process or kept stretched inside the container. One advantage conferred by fibers with a large anisotropy index is the ability to implant fibers with a large undeformed diameter through very small incisions or punctures. This allows the fiber to have a much smaller diameter in the delivery state than in the implanted state. This usually implies that the fiber in the delivery state is less hydrated than the fiber in the implanted state. This can be achieved by selection of the fluid medium. Anisotropy can be also utilized for fiber coiling, twisting or kinking upon exit from the introducer. Importantly, fibers with a bias toward spontaneous kinking or coiling can form an entangled mass even in a free space, independently of meeting any tissue resistance.

The container may be filled with a substantially non-toxic fluid medium (such as water, isotonic, hypotonic or hypertonic salt solutions, glycerol, poly(ethyleneglycol), vegetable oil, silicone oil or mineral oil). Any pharmaceutically acceptable aqueous or non-aqueous medium may be utilized in connection with the fiber. For example, a hydrogel fiber maintains a certain hydration level in equilibrium with this medium. This equilibrium can be said to define the "Delivery state". Partially dehydrated hydrogel is smaller in its volume, and stiffer than in a fully hydrated state. In addition, partially dehydrated hydrogels are able to maintain a "frozen deformation" that is released due to continuing hydration. This results in anisotropy indices larger than 1, i.e., in preferential swelling in radial direction and much smaller swelling, or even a shrinkage, in the axial direction. Large anisotropy index is an advantage for minimizing the incision for implantation. Besides, the reduced axial expansion is an advantage in some applications, such as in subdermal or intradermal injections. Axial shrinkage can cause retraction of the end of the fiber into the target tissue so that the entrance wound or puncture can close upon itself and heal cleanly. These criteria are also applicable to polymers which are capable of absorbing liquids which are not hydrogels.

Once the fiber is deposited into the tissue it rapidly achieves a thermal and osmotic equilibrium state with respect to body fluids present in the implantation site. The speed of the equilibration process depends, in part, on the nature of the composition of the fiber and fiber thickness. In this state (hereinafter referred to as the "Implanted State") the fiber achieves certain hydration, anisotropy index, diameter and length. These fiber characteristics are generally different in Delivery State and Implanted State. Generally speaking, hydration in the Implanted State may be the same, higher or lower than in the Delivery State. Preferably, hydration in the Implanted State is the same or higher than in the Delivery State. In the case that hydration does not change between the Delivery and

Implantation States, fiber is in the state of osmotic equilibrium with the tissue while still in the container and, hence, also at the moment of the initial contact with the tissue. Such situation is sometimes preferred from the viewpoint of biocompatibility and predictability of the outcome of the shape of the implant.

If the hydration increases between Delivery and Implantation States, the fiber expands and occupies larger volume in the implantation site than in the container. The diameter of the fiber also increases during implantation and the anisotropy index preferably decreases from a positive value in Delivery State to value equaling 1 in the Implanted State. This is preferred for minimally invasive implantation through a small-bore orifice as well in situations where implants according to the present invention generate a radial swelling pressure. The implant can also perform mechanical work leading to tissue expansion in a desirable extent and direction.

The fiber can be dispensed by a pressure generated in the fluid medium. This can be achieved in various ways. The pressure can be generated by a piston (such as a plunger in a syringe) or by liquid pressure such as hydrostatic pressure or gas pressure. The fiber itself also forms a "continuous piston" or a "continuous plunger" inside the channel and prevents the fluid from escaping into the implantation site. In this manner, a mechanical advantage is generated by hydraulic or pneumatic force which causes the fiber to be propelled out of the channel under relatively high pressure. "Channel" is meant to include that part of the lumen with a cross-section smaller than the cross-section of the undeformed fiber. In some cases, the channel is as long as the introduced fiber while in other cases it is shorter than that. The channel can be very short and narrow, such as a "lip" at the very end of the introducer. Such a short channel or lip can be relatively soft and deformable by the fiber pressure. The fiber and the channel can partially deform at the same time. This is advantageous particularly for relatively stiff fibers, such as fibers from substantially dehydrated hydrogels.

Fibers utilized in accordance with the present invention may be partly or fully dehydrated as long as they are sufficiently flexible to be deployed without fragmentation. Furthermore, their shape, diameter and deformability should be selected to substantially fill the orifice or channel. Accordingly, fibers should substantially comply with the shape of the orifice. In this manner, the fiber seals the orifice and does not allow for penetration of significant amounts of the pressurized fluid from the container, i.e., the fiber and orifice form a substantially fluid tight seal. In general, the fiber, the channel, the orifice and the fluid should cooperate to allow pressure to be maintained and propulsion of the fiber out of the orifice into the implant site. Those skilled in the art will readily determine fiber diameter suitable for a given delivery system (or vice versa). As mentioned above, to facilitate insertion into the channel, a fiber having a diameter less than the diameter of the channel may be inserted into the channel in a partially or fully unswelled,e.g., deliquified state, and then allowed to imbibe fluid contained in the container. As fluid is imbibed, the fiber swells and forms a substantially fluid-tight seal with the channel. The fiber may also be stretched to decrease its diameter in order to facilitate insertion into the channel. After insertion, the fiber may swell, e.g., by imbibing of liquid. Alternatively,

exposing the fiber to heat can cause it shorten while increasing in diameter to form a substantially fluid-tight seal.

The fiber should have suitable length, typically more than about 10x its diameter and, even more preferably, more than about 100 times its diameter in the state as to be found inside the container. If the fiber is very long (e.g., more than about 1000x its diameter) then the fiber inside the container is preferably arranged in a helix or on a reel or a spool so that it can freely unwind before entering the orifice. The fiber diameter in the Delivery State can vary, e.g., from several microns to about 1 mm or more. The fiber diameter in the implanted state is generally between about 20 microns to about 3 mm or more, but more typically between about 100 microns and about 1 mm. The diameter of the fiber in the fully hydrated state may range generally between about 100 microns and about 15 mm, but more usually between about 250 microns and about 2 mm. The length of the fiber may range from about 5mm to 10 meters, or more, depending on the size of the container and the device used to hold it there, e.g., a spool. It should be understood that these dimensions are only exemplary and those skilled in the art may vary them based on the needs of a particular procedure and the capacity of the introducer.

Once implanted into a preexisting cavity, the fiber usually forms a random bundle or clump (also referred to herein as a cluster) that is or becomes embedded in the tissue or at least partially fills the body cavity. In the case of a hydrogel, the fibrous cluster is surprisingly stable and resistant to untangling or migration through the tissue. This is major advantage over implantation of hydrogels in both particulate form and fibrous balls created according to the prior art. Stability of the fibrous cluster is primarily caused by fiber entanglement. Such entanglement can be further enhanced by coiling, twisting and kinking of the fiber during rehydration as various parts of the fiber rehydrate unevenly. The kinking and twisting can be enhanced by use of bi- or polycomponent hydrogel fibers composed of several hydrogels with different swelling capacities and expansion rates upon rehydration. In another embodiment, shape memory hydrogels and polymers are utilized. In this embodiment fiber(s) with preset coiled, kinked, twisted or braided shape that are straightened prior to or during the implantation. For instance, the fiber can be dried in a fixture that changes the fiber geometry. The fiber then returns to its original shape after rehydratation. Such a fiber has a bias to coil or kink or braid into a strongly entangled fibrous matrix. The matrix is stabilized by entanglement or braiding of fiber sections that it cannot be untangled easily. The cluster can also be stabilized by the tendency of hydrogel surfaces to adhere osmotically each to other in a partially hydrated state. This osmotic adhesion can be achieved, for instance, by expansion of dehydrated hydrogel fibers in or into a restricted space. The fiber surface can be treated to promote the mutual adhesion.

The fibrous cluster can be further stabilized and anchored into the tissue due to interaction with body fluids and cells. This includes clot formation, tissue capsule formation, and ingrowth of tissue. The fibrous cluster thus forms a matrix or scaffolding for tissue regrowth and regeneration. Surface properties of the fiber may support colonization by certain cells, adsorption of certain proteins, extracellular matrix substances and the like. This colonization can be supported by injection of suitable tissue-

cultured cells, such as fibroblasts, chondrocytes or stem cells relevant to the implant site. Such cells can be injected prior to, simultaneously with or after the fiber injection. The fiber surface can be selected and/or treated to support cell adhesion and spreading. It is also possible to implant at least two types of fibers, e.g., one being hydrogel that does not support the cell adhesion and growth, and the other fiber from a material that supports cell adhesion and growth. Such fibers can be co-extruded or implanted sequentially. At least one of the fibers can be made from a biodegradable material.

The fluid medium in the container may be a gas or a liquid. In the case of gas, the gas may be a mixture of gases (air, nitrogen, carbon dioxide etc) and saturated by water vapors in equilibrium with the fibers inside the container. Preferred fluid medium is a liquid. Although it is preferred that the fluid should not penetrate into the tissue in significant quantity, the fluid should still be substantially non-toxic. The liquid may be aqueous or non-aqueous. For example, the liquid may be an oil such as mineral oil or vegetable oil. Preferred is an aqueous liquid. Examples are water, isotonic salt solution, hypertonic salt solution, diluted alcohol solution, aqueous glycerol solution, DMSO, etc. The liquid is preselected to achieve the desired fiber properties in the delivery state. This type of control of hydrogel properties, particularly degree of hydration, is well known to those skilled in the hydrogel art.

If the fiber is injected in its dehydrated delivery state into a tight cavity whose volume is smaller than the volume of injected fibers at implanted hydration, then the fibrous cluster can be very compact with tightly packed fibers and a relatively low amount of interstitial spaces. Fibers that cannot achieve their full hydration equilibrium because of the spatial restriction will adhere firmly one to another. Such a cluster can approximate the character of a solid elastomeric body.

In one embodiment, the fiber is injected together with living cells that will colonize the spaces within the fibrous matrix and form appropriate tissues. The injection of cells and injection of fibers is achieved preferably through two different channels. In this case the fluid medium is preferably a balanced isotonic solution. Suitable cells may be, e.g., autologous and/or allogenic chondrocytes, fibroblasts, stem cells and the like. Fiber surfaces may be modified to promote cell adhesion. It is known that healing is promoted by growth factors and other biochemicals, and cells may act as a "live delivery system."

Sterility of the fiber and propulsion fluid is preferred for tissue augmentation. The sterilization of a whole implantation system according to the present invention can, in certain embodiments, be achieved in combination with a hydrogel in contact and in the equilibrium with the propulsion fluid. Sterilization is usually one of the last steps in preparing the system for implantation. The sterile system may then be stored in a state of readiness for use. In other embodiments, it is preferred to sterilize the fiber in its dehydrated state, preferably placed within the delivery system but separated from the sterile propulsion fluid. The two components are then combined prior to implantation. This system generally improves the shelf stability of the fiber and is particularly useful for hydrogels sterilizable in dehydrated state.

Manufacturing techniques for making fibers are well known to those skilled in the art. It is contemplated that any well known technique may be used to prepare fibers for use in connection with the present invention. For example, hydrogel fibers can be manufactured by dry spinning of hydrogel melts, extrusion or other known techniques. A particularly advantageous production method is wet spinning by extrusion of a polymer solution in a water-miscible solvent into an aqueous coagulation bath followed by washing of the fiber and processing into the injectable form. This method yields fibers with highly wettable and lubricious surfaces very suitable for this application. Some preferred fiber production methods are described in the following non-limiting examples.

Fibers, e.g., hydrogel fibers, according to the present invention are useful for various medical treatments such as for augmentation of tissues such as spinal disc, urinary sphincter or skin. For example, an injectable hydrogel system according to the present invention can be used for augmentation of Nucleus Pulposus (*NP*). In a healthy disc, *NP* facilitates active transport of nutrients in, and metabolites out of the disc living tissues (i.e., Annulus Fibrosus, endplate cartilage and Nucleus Pulposus itself). Nutrients and metabolites are pumped due to the periodical dehydration and rehydration of *NP* under varying load in prone and upright body positions. Disc degeneration cascade seems to be initiated by desiccation of the *NP*. With advancing age, *NP* gradually loses its capability to bind water, perhaps due to the shift of the balance between production of glycoproteins and proteins such as collagen. As the *NP* loses its capability to bind sufficient amount of water, swelling pressure generated by *NP* decreases due to the loss of osmotic pressure generated by the hydrophilic proteoglycan components. Desiccation of *NP* can thus directly lead to the loss of intra-discal pressure, which, in turn, leads to the loss of disc height. These conditions lead to anomalous modes of deformation in the annulus fibrosus (*AF*) which then starts to split and delaminate. At the same time, loss of disc height and loss of *NP* hydrophilicity interferes with the active transport of nutrients and metabolites in the disc. Insufficient nutrient transport leads to further degradation of *NP* tissue which is manifested as even larger decrease of the liquid-holding capability by *NP*, and even larger decrease in disc height. Loss of liquid-binding capability thus starts the cascade leading to the disc degeneration and its ultimate destruction.

This cascade can be stopped or even reversed according to the present invention by injection of hydrogel fibers into the desiccating disc. The hydrogel fiber implant supplements the water-binding capability of the natural *NP*, which, in turn, helps to restore nutrient and metabolite exchange. The restored transport leads to regeneration of the living intradiscal tissues to slow down (or even reverse) the disc degeneration process. Contrary to other surgical intervention in the later stages of the disc degeneration process (such as replacement of nucleus, replacement of the whole disc, or spine fusion), injection of a hydrogel into the disc is possible using minimally invasive methods through a very small incision, or even through a needle puncture in *AF*. Injection of partially or fully dehydrated hydrogel fibers does not necessarily require nucleotomy, i.e., removal of at least a part of *NP*. The dehydrated hydrogel fibers share water with the residual tissue just after the injection. Hydrogel then attracts more water through the endplates to increase its hydration. The resultant volume increase generates an increased

intradiscal pressure and leads to the increased disc height. Both beneficial changes then lead to more natural modes of deformation of *AF* as well to restarted load-driven transport of nutrients and metabolites. Implantation of hydrogel fibers is also appropriate after a percutaneous nucleotomy is performed to remove desiccated NP. Although injection of the fiber(s) is conducted under relatively high pressure as defined herein, care should be taken to insure that pressure is low enough to be able to control the speed and amount of fiber being deposited into the disc space so as not to overfill the space.

Generally speaking, the dehydrated hydrogel implanted into the disc can have various forms. Particularly advantageous are forms of continuous fibers, rods or long loops or rings that can be injected in a straight geometry through a hypodermic needle. Once injected, their geometry changes into an expanded, kinked and/or entangled form that cannot be readily extruded back through the implantation incision. Such forms are advantageous in their resistance to migration to various sites in the body. Advantageously, the hydrogel is injected in a partly or fully dehydrated state to occupy a minimum volume and to provide maximum expansion due to its rehydration. It should be understood that fibers other than hydrogel fibers can be used in connection with intradiscal implants.

Some preferred uses are described in the following non-limiting examples. The examples have been included for purposes of exemplifying certain aspects of the present invention and are not intended to serve as limitations of any sort.

EXAMPLE 1

One particular form of temporarily dehydrated hydrogel can be prepared as follows. The multi-block acrylic copolymer is prepared into the form of a stable spinning solution according to U.S. Patent No. 6,232,406. The hydrogel selected for this example has equilibrium liquid content 90% by weight in isotonic saline solution. The polymer solution was filtered through a 0.4 micron filter and charged into a pressurized jacketed vessel. Pressurization is achieved by compressed nitrogen that extrudes the solution through a metering gear pump into a nozzle. The nozzle is immersed in an aqueous coagulation bath, in this case consisting of 0.9% NaCl solution with a small concentration of NaSCN, usually less than 1% by wt. An extruded stream of the polymer solution is guided into a horizontal glass coagulation tube through which the coagulation bath flows by a constant rate. The polymer solution coagulates in the tube while being carried by the liquid stream. The reason for this arrangement is prevention of any contact of the still-liquid solution stream with any solid object. A spinneret 9 and extruded fiber 10 carried away through the coagulation tube 11 are illustrated in FIG. 5.

Coagulated fiber is washed on the rest of the path through the bath to remove the major part of the NaSCN solvent. Substantially washed hydrogel fiber is then wound on a perforated spool with a slight extension (approx. 150% of its relaxed length) due to its elasticity. The fiber is deposited in a single layer to facilitate the subsequent operations. Its liquid content is approx. 95% at this stage. Ends of the fiber are then secured to the

spool and washed in an excess of isotonic saline until all detectable NaSCN is removed. The relaxed diameter of the fiber is approximately 2 mm at this stage.

Washed hydrogel fiber is then immersed into an excess of 1 % by wt. phosphoric acid for 4 hours and washed overnight in deionized water until all free acid is removed. Hydration of the hydrogel decreases by the acid treatment to less than about 50% by weight. Without wishing to be bound by any particular theory, it is believed that the acidification suppresses ionization of carboxylate groups and causes formation of an internal salt between pendant carboxyl groups and pendant amidine groups.

The fiber is then tightly rewound on a slightly conical stainless steel rod of 10 mm diameter (maximum value) and dried at 70°C. Consequently, the fiber shrinks and tightens on the spool. Then the fiber is dried at ambient temperature for two hours and at 50°C for another 1 hr. Further shrinkage tightens and orients the fiber. Dry fiber has a diameter approximately 0.15 mm. Dry fiber helix (its shape resembles the shape in FIG. 4C) is then carefully stripped from the rod and inserted into the introducer depicted in FIG. 6. The body of the helix is inserted into the plastic syringe **C** while the straight end of the dry fiber is threaded through the 3-way connector **B** with Luer locks and into the catheter **D** with the hypodermic needle **E** at its end. (The needle **E** has smaller internal diameter than the catheter **D**, forming thus a channel where the fiber is compressed in proximity to the outlet). Dry fiber is inserted through the hypodermic needle so that its end protrudes from the needle tip. Another syringe **A** filled with sterile isotonic saline *p.i.* (*pro injection* or injectable isotonic saline) is attached to the outlet of **B** that is equipped with a cock.

The assembly is then sealed and sterilized. Prior to fiber implantation, the valve of outlet B is opened and sterile saline is transferred from syringe A into the syringe C containing the dry fiber helix. The fiber swells by hydration, softens and fills the lumen of the hypodermic needle. The protruding end of the fiber is cut off. The hydrogel fiber is now ready for injection into the intradiscal space.

Once the fiber is injected through the Annulus Fibrosus into the Nucleus Pulposus, the needle **E** is withdrawn and the access wound is closed. The fiber in the disc now swells as the body fluid neutralize the acidified fiber so that its full hydration increases back from about less than 50% (w) to more than 80% by weight. This process is relatively slow since it is dependent on penetration of additional water into the NP.

EXAMPLE 2

Injectable fibers can be used also for subcutaneous dermal filling of deep wrinkles or other cosmetic defects. The fibers from the Example 1 are, prior the acidification step, rewound on a stainless steel drying frame and dried. The dry fiber is cut into sections of various lengths between 25 to 250 mm and inserted into hypodermic needles. The excess of the fiber is removed. The needle is placed in a plastic protective sleeve and its connecting end is closed with a plastic plug. The assembly is then sealed in a plastic pouch and gamma sterilized.

Prior to the utilization, the needle is unplugged and connected to a syringe containing sterile isotonic saline solution. The solution is pushed into the needle to allow hydration of the hydrogel fiber. Once the fiber is sufficiently hydrated, the needle is inserted into a subdermal site and the hydrogel fiber is extruded by pressure of the saline. Fiber extrusion is shown in FIG. 7. The hydrated fiber has outside diameter larger than inside diameter of the needle. FIG. 7 shows the fiber's inclination to coil due to its decompression upon egress from the needle.

EXAMPLE 3

The hydrogel implantable fiber can be also prepared according to US Patent 4,663,358 hereby incorporated by reference. A solution of fully hydrolyzed PVA in a mixture of water and glycerol is pulled into hypodermic needles and retained in the needle bores by plastic plugs. Needles are placed into plastic pouches and frozen to -20°C. The PVA solution solidifies to a firm gel, thus forming a hydrogel fiber inside the needle. The packaged needle is then radiation sterilized. Prior to utilization, the needle is unplugged and connected to a syringe containing sterile isotonic saline solution. The needle is inserted into the target tissue and the hydrogel fiber is extruded by pressure of the saline into the implantation site. The target tissue can be dermis, cornea, urinary sphincter and the like.

EXAMPLE 4

A sterile solution of hot agarose is pulled into a sterile hypodermic needles and retained in the needle bores by sterile plastic plugs. Cooling to ambient temperature causes solidification of the solution into a hydrogel and formation of an elongate fiber having the shape of the internal bore of the needle. Needles filled with hydrated hydrogel fibers are then placed into semipermeable plastic pouches and sterilized by ethylene oxide. Prior to utilization, the needle is unplugged and connected to a syringe containing sterile isotonic saline solution. The needle is inserted into the target tissue and the hydrogel fiber is extruded by pressure of the saline into the implantation site. The target tissue can be dermis, cornea, urinary sphincter and the like.

EXAMPLE 5

Hydrogel fiber of fully hydrated diameter about 5 mm is produced by spinning polymer solution into a coagulation bath as described in the Example 1. The fiber washed in isotonic saline was pre-stretched on plastic frames and dried first at ambient conditions and then at an elevated temperature. The dehydrated fiber had diameter about 1.5 mm. The fiber is cut into sections about 20 to 30 mm long and one end sharpened by grinding. The resulting xerogel "needles" are packaged into pouches and radiation sterilized.

The needles are implanted into Nucelus Pulposus tissue through a puncture though the AF. One or more needles per disc are pushed by the sharp end first through the introducer with aid of a pushing rod. If more than one needle per disc is used, each needle may be implanted through the same or different incision and can be implanted in various angles. Once in the NP tissue, the needles are advantageously turned sideways from the entry point using the pusher rod and introducer is withdrawn. Xerogel needles swell due to hydration and increase their diameter at least 3 times while decreasing their length by up to 20%. This anisotropic swelling leads to a short, stubby cylinder that cannot readily escape through the original entry puncture.

EXAMPLE 6

Hydrogel solution according to the Example 1 is cast into a circular mold to form a flat ring of about 20 mm inner diameter and 5 mm wide. The hydrogel ring is stretched on two pins about 30 mm apart and dried. The dry ring forms a rigid rod-like shape of approximately circular cross-section. The rod is packaged and sterilized. It is implanted into the NP tissue in the left-right orientation (along the long axis of the disc). By swelling the implant expands and attempts to resume a ring configuration that does not fit into the incision in the annulus fibrosus.

EXAMPLE 7

A multi-block acrylic copolymer is prepared into the form of a stable spinning solution according to U.S. Patent No. 6,232,406. The hydrogel selected for this example has conversion of hydrolysis approximately 25 molar % and equilibrium liquid content approximately 75% by weight in isotonic saline solution. Hydrogel fiber or rod is prepared by extrusion of the solution into water coagulation bath and washed thoroughly by water. Its hydrated diameter in water is approximately 5 mm. The fiber is then cut length-wise in selected sections about 5 mm long and about 50 mm apart. The fiber is then fixed to a plastic frame and dried. Dry fiber on the frame is then immersed into 10% solution of NaOH until its surface turns red. The red in color indicates reaction of nitrile groups. The exterior is more colored than the core indicating a gradient of concentration of newly formed groups. The resulting hydrogel rod is then thoroughly washed in isotonic saline and dried to a diameter of about 1.5 mm. The rod is then cut into parts about 40 mm long, each part containing one longitudinally cut section at one end. The other end is sharpened into a needle shape.

The above description sets forth preferred embodiments and examples. It should be understood that those skilled in the art will envision modifications of the embodiments and examples that, although not specifically stated herein, are still within the spirit and scope of any claims which may be appended hereto.

What is claimed is:

1. A fiber implant delivery system which comprises:

an introducer including an internal lumen and a constricted discharge orifice in communication with the internal lumen, the discharge orifice having an internal dimension; and

a deformable fiber having an external dimension which is greater than the internal dimension of the discharge orifice when the deformable fiber is fully expanded, the deformable fiber being positioned within the internal lumen in slidable and substantially fluid tight engagement with the internal dimension of the discharge orifice such that pressurization of fluid contained within the lumen causes the fiber to move through the discharge orifice and into tissue.

2. A fiber implant delivery system according to claim 1 wherein the introducer further includes a container in communication with the internal lumen.

3. A fiber implant delivery system according to claim 2 wherein the container is adapted to contain a portion of the fluid.

4. A fiber implant delivery system according to claim 3 wherein pressurization of the fluid is caused by a plunger slidably mounted within the container.

5. A fiber implant delivery system according to claim 1 wherein pressurization is caused by compressed gas.

6. A fiber implant delivery system according to claim 1 wherein the fiber is a hydrogel.

7. A fiber implant delivery system according to claim 1 wherein the internal lumen and constricted discharge orifice are contained in a hypodermic needle.

8. A fiber implant delivery system according to claim 1 wherein the internal lumen and constricted discharge orifice are contained within a catheter.

9. A fiber implant delivery system according to claim 2 wherein the container is adapted to contain a portion of the fiber.

10. A fiber implant delivery system according to claim 9 wherein the fiber is contained in the container in a storage configuration selected from the group consisting of zig-zag transverse to the internal lumen, zig-zag parallel to the internal lumen, single layered helix, double layered helix and coiled.

11. A fiber implant delivery system according to claim 9 wherein the fiber is contained on a spool located in the container.

12. A fiber implant delivery system according to claim 1 wherein the fluid is selected from the group consisting of gas, water, isotonic salt solution, hypotonic salt solution, hypertonic salt solution, glycerol, glycerin, polyethylene glycol, polypropylene glycol, vegetable oil, silicone oil, mineral oil, DMSO, dilute alcohol and combinations thereof.

13. A fiber implant delivery system according to claim 1 wherein the fluid contains a medicinal agent.

14. A fiber implant delivery system according to claim 1 wherein the internal lumen and constricted discharge orifice each have a substantially similar internal cross-sectional dimension.

15. A fiber implant delivery system according to claim 1 wherein the interior dimension of the discharge orifice or the internal lumen is deformable and capable of expanding radially in response to pressure generated by the fiber cross-section.

16. A fiber implant delivery system according to claim 1 wherein the fiber includes a radiopaque material.

17. A fiber implant delivery system which comprises:

an introducer including an internal lumen and a constricted discharge orifice in communication with the internal lumen, the discharge orifice having an internal dimension; and

a fiber positioned within the internal lumen, the fiber having a cross-sectional dimension greater than the internal dimension of the discharge orifice whereby passage of the fiber from the lumen through the discharge orifice in response to a force on the fiber causes the cross-sectional dimension of the fiber to decrease and increase the rate of velocity of the fiber within the constricted orifice to thereby facilitate direction of the fiber into tissue.

18. A fiber implant delivery system according to claim 17 wherein the force is applied hydraulically or pneumatically by means of a fluid in contact with the fiber.

19. A fiber implant delivery system according to claim 18 wherein the introducer further includes a container in communication with the internal lumen.

20. A fiber implant delivery system according to claim 19 wherein the container is adapted to contain a portion of the fluid.

21. A fiber implant delivery system according to claim 20 wherein pressurization of the fluid is caused by a plunger slidably mounted within the container.

22. A fiber implant delivery system according to claim 18 wherein the force is caused by compressed gas.

23. A fiber implant delivery system according to claim 17 wherein the fiber is a hydrogel

24. A fiber implant delivery system according to claim 17 wherein the fiber includes a radiopaque material.

25. A fiber implant delivery system according to claim 17 wherein the internal lumen and constricted discharge orifice are contained in a hypodermic needle.

26. A fiber implant delivery system according to claim 17 wherein the internal lumen and constricted discharge orifice are contained within a catheter.

27. A fiber implant delivery system according to claim 19 wherein the container is adapted to contain a portion of the fiber.

28. A fiber implant delivery system according to claim 27 wherein the fiber is contained in the container in a storage configuration selected from the group consisting of zig-zag transverse to the internal lumen, zig-zag parallel to the internal lumen, single layered helix, double layered helix and coiled.

29. A fiber implant delivery system according to claim 27 wherein the fiber is contained on a spool located in the container.

30. A fiber implant delivery system according to claim 18 wherein the fluid is selected from the group consisting of gas, water, isotonic salt solution, hypotonic salt solution, hypertonic salt solution, glycerol, glycerin, polyethylene glycol, polypropylene glycol, vegetable oil, silicone oil, mineral oil, DMSO, dilute alcohol and combinations thereof.

31. A fiber implant delivery system according to claim 18 wherein the fluid contains a medicinal agent.

32. A fiber implant delivery system according to claim 17 wherein the internal lumen and constricted discharge orifice each have a substantially similar internal cross-sectional dimension.

33. A fiber implant delivery system according to claim 17 wherein the interior dimension of the discharge orifice or the internal lumen is deformable and capable of expanding radially in response to pressure generated by the fiber cross-section.

34. A fiber implant for insertion into soft tissue comprising at least one anisotropic hydrogel fiber.

35. A fiber implant according to claim 34 wherein the hydrogel fiber is a shape memory hydrogel.

36. A fiber implant according to claim 34 wherein the hydrogel fiber is anisotropic due to inherent variable rates of hydration.

37. A fiber implant according to claim 34 wherein the fiber is twisted, kinked and entangled with itself.

38. A fiber implant according to claim 34 wherein the hydrogel fiber contains a hydrogel having an equilibrium content of at least about 30% to about 97% by weight of liquid in a state of full hydration by 0.9% by weight NaCl solution.

39. A fiber implant according to claim 38 wherein the hydrogel fiber contains a hydrogel having an equilibrium content of at least about 50% by weight of liquid in a state of full hydration by 0.9% by weight NaCl solution.

40. A fiber implant according to claim 38 wherein the hydrogel fiber contains a hydrogel having an equilibrium content of at least about 80% by weight of liquid in a state of full hydration by 0.9% by weight NaCl solution.

41. A fiber implant according to claim 34 wherein the hydrogel fiber includes a derivative of polyacrylic acid.

42. A fiber implant according to claim 41 wherein the derivative of polyacrylic acid includes a product of a controlled partial reaction of nitrile groups in polyacrylonitrile.

43. A fiber implant according to claim 42 wherein the partial reaction is hydrolysis or aminolysis of polyacrylonitrile.

44. A fiber implant according to claim 43 wherein the partial reaction is base-catalyzed hydrolysis of polyacrylonitrile.

45. A fiber implant according to claim 34 wherein the hydrogel fiber includes a polymer selected from the group consisting of polyvinyl alcohol, agarose, agarose derivative and alginate.

46. A fiber implant according to claim 34 wherein the hydrogel fiber preferentially expands along its radial axis.

47. A fiber implant according to claim 34 wherein the hydrogel fiber includes a hydrogel having from about 1% (mol) to about 50% (mol) of carboxylate groups.

48. A fiber implant according to claim 47 wherein the hydrogel fiber includes a hydrogel having greater than about 10% (mol) of carboxylate groups.

49. A fiber implant according to claim 34 wherein the hydrogel fiber is plasticized by a water-miscible liquid comprising a liquid selected from the group consisting of DMSO, glycerol, polyethylene glycol, polypropylene glycol and sugar/water.

50. A fiber implant according to claim 34 wherein the hydrogel fiber includes a hydrogel which has gradient of composition and swelling with maximum swelling on its surface.

51. A fiber implant according to claim 45 wherein the hydrogel fiber contains a high concentration of ionizable acidic groups on its surface.

52. A fiber implant according to claim 49 wherein the hydrogel fiber ionizable acidic groups are selected from the group consisting of carboxylates and sulphates.

53. A fiber implant according to claim 32 wherein the hydrogel fiber is a polycomponent fiber comprising at least two swellable polymers having different respective swelling capacities.

54. A fiber implant according to claim 32 wherein the hydrogel fiber preferentially shrinks along its axial axis.

55. A fiber implant according to claim 34 wherein the hydrogel fiber includes a medicinal agent.

56. A fiber implant according to claim 34 wherein the hydrogel fiber includes a radiopaque material.

57. A fiber implant according to claim 34 wherein the hydrogel fiber has two ends which are connected to form a continuous ring.

58. A method for dispensing a fiber implant to a target site in tissue comprising:

providing an introducer including an internal lumen and a constricted discharge orifice in communication with the internal lumen, the discharge orifice having an internal dimension, the internal lumen containing fluid;

providing a deformable fiber having an external dimension which is greater than the internal dimension of the discharge orifice when the deformable fiber is fully expanded, the deformable fiber positioned within the internal lumen in slidable and substantially fluid tight engagement with the internal dimension of the discharge orifice;

inserting an end of the introducer into tissue at the target site;

pressurizing fluid contained within the lumen to cause the fiber to pass through the discharge orifice and into the target site wherein passage of the fiber through the discharge orifice causes a decrease in the diameter of the fiber.

59. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein passage of the fiber through the discharge orifice causes the fiber to partially expel fluid contained in the fiber.

60 A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein the fiber is a hydrogel.

61. A method for dispensing a fiber implant to a target site in tissue according to claim 59 wherein the fluid in the fiber is aqueous or oleaginous.

62. A method for dispensing a fiber implant to a target site in tissue according to claim 60 wherein the fluid in the hydrogel is aqueous and passage of the fiber through the discharge orifice causes partial dehydration of the fiber.

63. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein after passage of the fiber into the target site, the fiber increases in diameter through hydration.

64. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein after passage of the fiber into the target site, the fiber shrinks axially.

65. A method for dispensing a fiber implant to a target site in tissue according to claim 64 wherein the fiber shrinks axially due to shape memory.

66. A method for dispensing a fiber implant to a target site in tissue according to claim 63 wherein the fiber coils, kinks, twists and entangles itself to form a bundle.

67. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein the target site is a preexisting cavity in the tissue.

68. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein pressure exerted by the fluid on the fiber is sufficient to force the fiber into tissue, thus creating an implant at the target site.

69. A method for dispensing a fiber implant to a target site in tissue according to claim 59 wherein the fiber coils, kinks, twists, and entangles itself to form a bundle.

70. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein the target site is a disc space between adjacent vertebrae of a spine.

71. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein the fiber has two ends which are connected to form a continuous ring.

72. A method for dispensing a fiber implant to a target site in tissue according to claim 58 wherein the fiber includes a radiopaque material.

73. A method for manufacturing a fiber implant delivery device comprising:

providing an introducer including an internal lumen and a constricted discharge orifice in communication with the internal lumen, the discharge orifice having an internal dimension;

providing a deformable swellable fiber having a cross-sectional dimension greater than the internal dimension of the discharge orifice when the fiber is in a fully swelled state;

inserting one end of the swellable fiber into the lumen and at least partially through the constricted discharge orifice such that the diameter of the swellable fiber is decreased by compression from the constricted discharge orifice.

74. A method for manufacturing a fiber implant delivery device according to claim 73 wherein the fiber is made of hydrogel.

75. A method for manufacturing a fiber implant delivery device according to claim 73 wherein the introducer includes a plunger.

76. A method for manufacturing a fiber implant delivery device according to claim 73 further comprising adding a fluid to the internal lumen.

77. A method for manufacturing a fiber implant delivery device according to claim 76 wherein the fluid is selected from the group consisting of gas and liquid.

78. A method for manufacturing a fiber implant delivery device according to claim 77 wherein the liquid is aqueous or oleaginous.

79. A method for manufacturing a fiber implant delivery device according to claim 73 wherein the internal lumen and constricted discharge orifice each have a substantially similar internal cross-sectional dimension.

80. A method for manufacturing a fiber implant delivery device according to claim 73 wherein the internal dimension of the discharge orifice or the internal lumen is deformable and capable of expanding radially in response to pressure generated by the fiber cross-section.

81. A method for manufacturing a fiber implant delivery device comprising:

providing an introducer including an internal lumen and a constricted discharge orifice in communication with the internal lumen, the discharge orifice having an internal dimension;

providing a deformable swellable fiber in an at least partially unswelled state, but capable of having a cross-sectional dimension greater than the internal dimension of the discharge orifice when the fiber is in a fully swelled state, wherein the cross-sectional dimension of the at least partially unswelled fiber is smaller than the internal dimension of the discharge orifice;

inserting one end of the swellable fiber into the lumen and at least partially through the constricted discharge orifice; and

allowing the fiber to swell and form a substantially fluid-tight seal with the internal dimension of the discharge orifice.

82. A method for manufacturing a fiber implant delivery device according to claim 81 wherein the fiber is made of hydrogel.

83. A method for manufacturing a fiber implant delivery device according to claim 81 wherein the introducer includes a plunger.

84 A method for manufacturing a fiber implant delivery device according to claim 81 further comprising adding a fluid to the internal lumen.

85. A method for manufacturing a fiber implant delivery device according to claim 84 wherein the fluid is selected from the group consisting of gas and liquid.

86. A method for manufacturing a fiber implant delivery device according to claim 85 wherein the liquid is aqueous or oleaginous.

87. A method for manufacturing a fiber implant delivery device according to claim 81 wherein the internal lumen and constricted discharge orifice each have a substantially similar internal cross-sectional dimension.

88. A method for manufacturing a fiber implant delivery device according to claim 81 wherein the internal dimension of the discharge orifice or the internal lumen is deformable and capable of expanding radially in response to pressure generated by the fiber cross-section.

89. A method for dispensing a fiber implant to a target site in tissue comprising:
providing an introducer including an internal lumen and a constricted discharge orifice in communication with the internal lumen, the discharge orifice having an internal dimension, the internal lumen containing fluid;
providing an anisotropically deformable fiber positioned within the internal lumen in slidable and substantially fluid tight engagement with the internal dimension of the discharge orifice;
inserting an end of the introducer into tissue at the target site;
pressurizing fluid contained within the lumen to cause the fiber to pass through the discharge orifice and into the target site.

90. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein passage of the fiber through the discharge orifice causes a decrease in the diameter of the fiber.

91. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the fiber is a hydrogel.

92. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the fluid in the fiber is aqueous or oleaginous.

93. A method for dispensing a fiber implant to a target site in tissue according to claim 92 wherein the fluid in the hydrogel is aqueous and passage of the fiber through the discharge orifice causes partial dehydration of the fiber.

94. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein after passage of the fiber into the target site, the fiber increases in diameter through hydration.

95. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein after passage of the fiber into the target site, the fiber shrinks axially.

96. A method for dispensing a fiber implant to a target site in tissue according to claim 95 wherein the fiber shrinks axially due to shape memory.

97. A method for dispensing a fiber implant to a target site in tissue according to claim 94 wherein the fiber coils, kinks, twists and entangles itself to form a bundle.

98. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the target site is a preexisting cavity in the tissue.

99. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein pressure exerted by the fluid on the fiber is sufficient to force the fiber into tissue, thus creating an implant at the target site.

100. A method for dispensing a fiber implant to a target site in tissue according to claim 99 wherein the fiber coils, kinks, twists, and entangles itself to form a bundle.

101. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the target site is a disc space between adjacent vertebrae of a spine.

102. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the fiber includes a radiopaque material.

103. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the fiber includes a medicinal agent.

104. A method for dispensing a fiber implant to a target site in tissue according to claim 89 wherein the fiber has two ends which are connected to form a continuous ring.

FIG. 1A

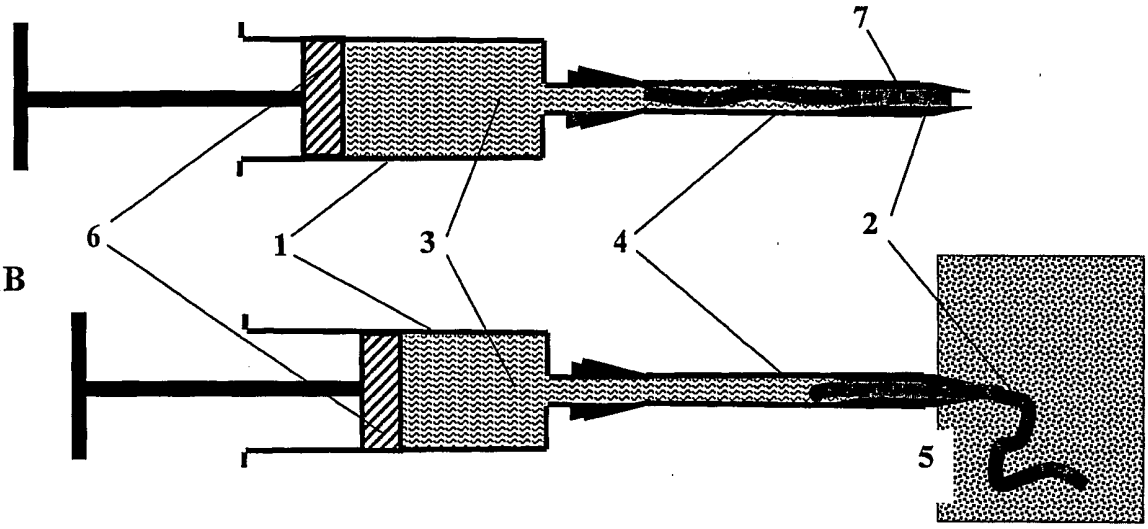


FIG. 1B

FIG. 2A

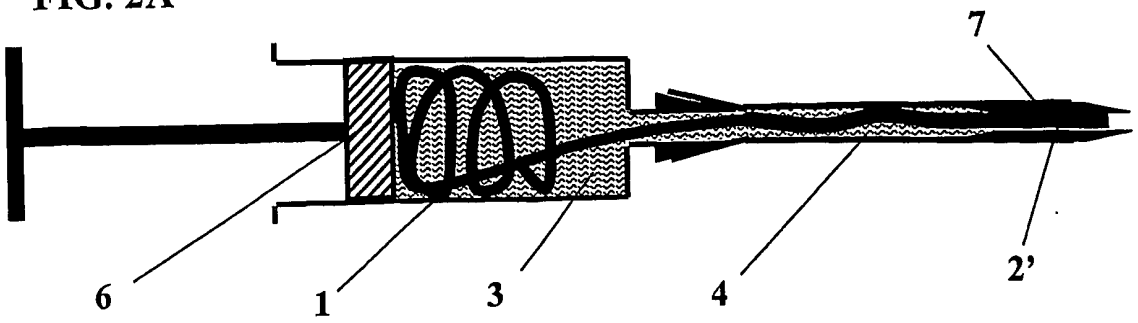


FIG. 2B

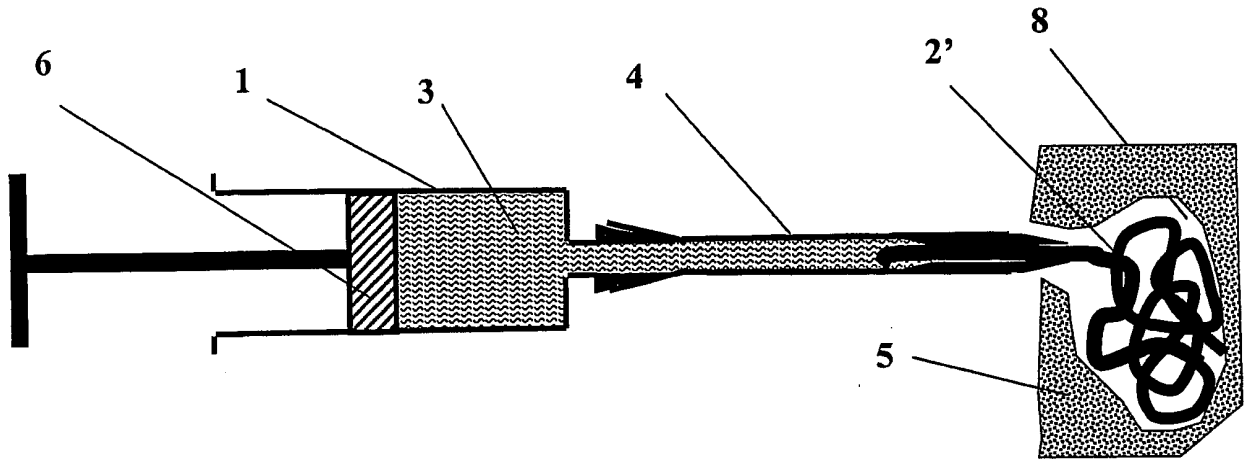


FIG. 3

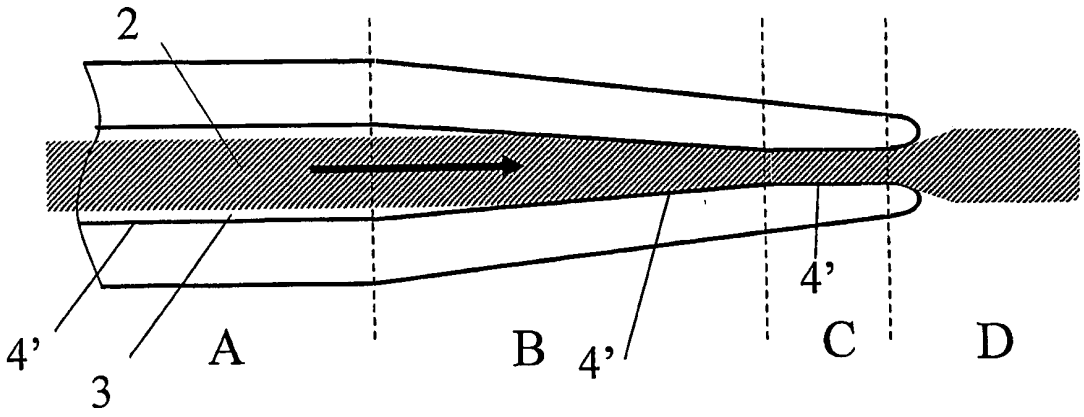


FIG. 4A

FIG. 4B

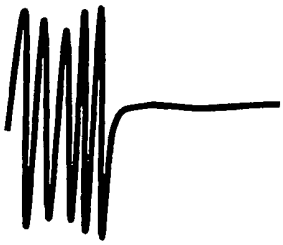


FIG. 4C

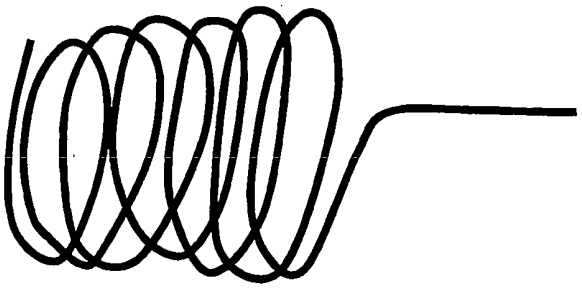
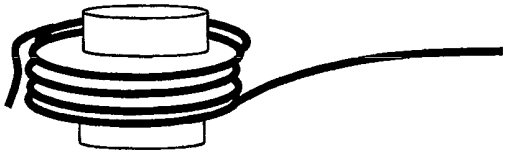


FIG. 4D



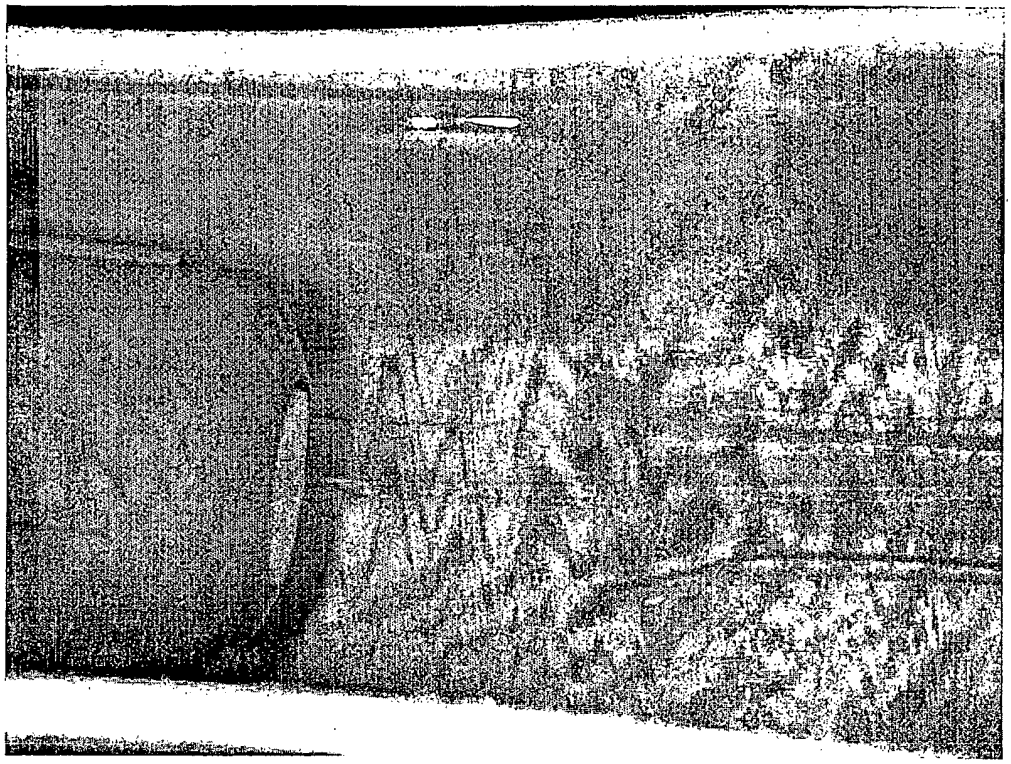


FIG. 5

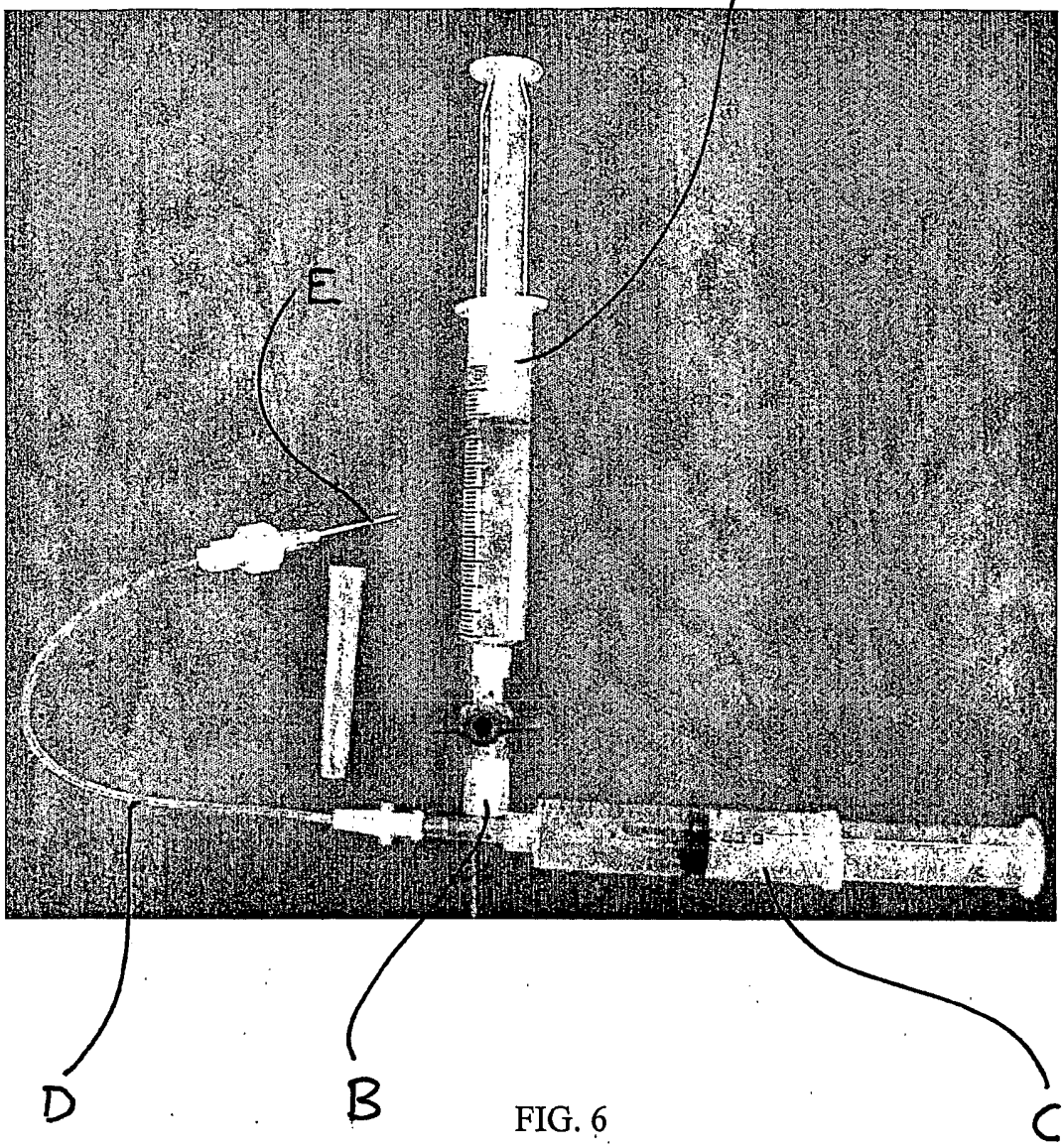


FIG. 6

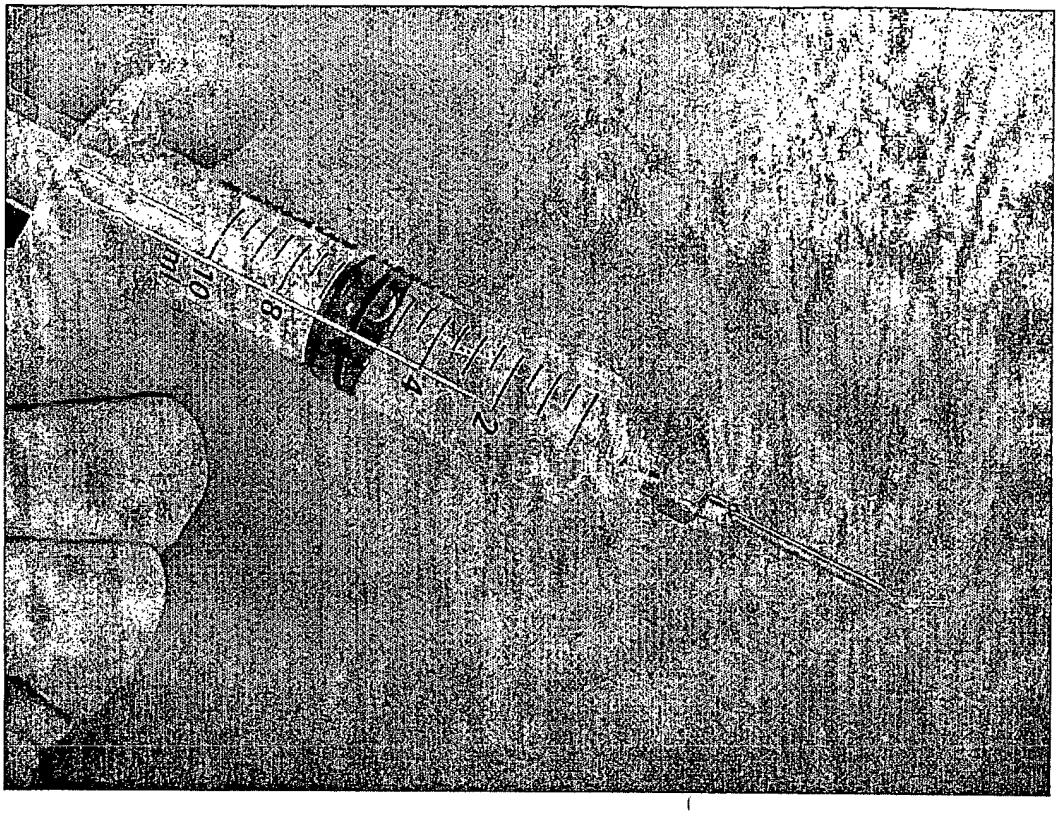


FIG. 7